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Title: Modulators of Bruton's Tyrosine Kinase and Bruton's Tyrosine Kinase Intermediates and Methods for Their Identification and Use in the Treatment and Prevention of Osteoporosis and Related Disease States

# Bone Mineral Density of the Proximal Tibia in Wild Type and Btk Knockout Mice

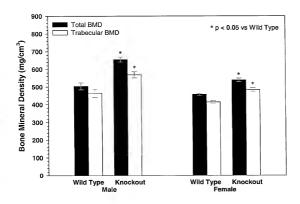


Figure 1.

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# Bone Mineral Density of the Proximal Tibia in Wild Type and Btk<sup>xid</sup> Mice

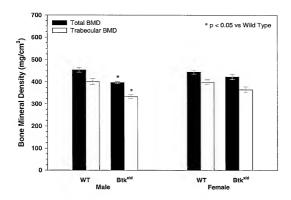


Figure 2.

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## Female Mice with Btklo Transgene

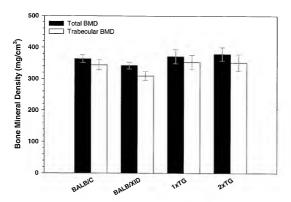


Figure 3.

### **BTK Constructs**

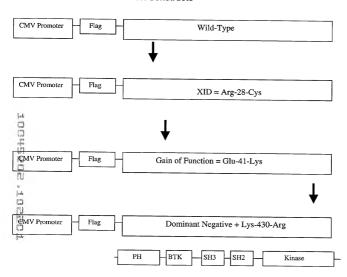
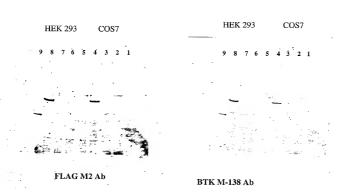


Figure 4.

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## Mu BTK wt tagged/untagged HEK/COS transient Western



Legend:

Lanes 1 and 5: pcDNA

Lanes 2 and 6: BTK wt/pcDNA

Lanes 3 and 7: p3XFLAG Lanes 4 and 8: BTK wt/p3XFLAG

Lane 9: BAP FLAG control

Figure 5.

# BTK-FLAG mutant RAW 264.7 stable mix whole cell lysates

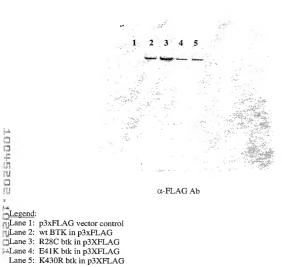


Figure 6.

Legend:

Wild-Type BTK

### **Phosphorylation Analysis of BTK Mutants**

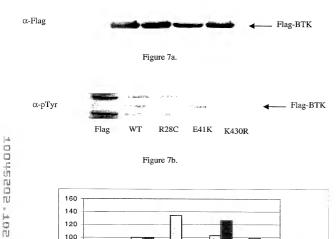


Figure 7b.

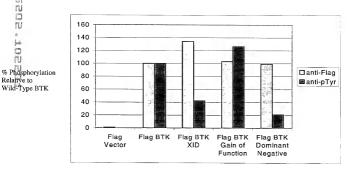


Figure 7c.

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# Total Tyrosine Phosphorylation Vector WT XID G of F DN

Figure 8.

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# BTK mutant immunoprecipitation kinase assays (stable pools, unstimulated)

R28C (xid rBTK SLP76 Mock IP Vector Wild Type mutant) E41K K430R

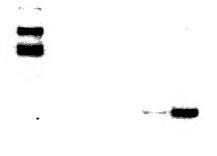


Figure 9.

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### Actin staining of Btk/RAW cell stable cell lines

Btk wt

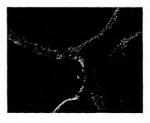


Figure 10a.



Figure 10b.

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### E41K-gain of function



Figure 10c.